

To The July 14, 2004 Office Action) -- September 3, 2004]

REMARKS

After entry of the complete listing of the claims provided above:

Claims now pending in this application include: claims 826, 828-832, 835-847, 849-856, 858-862, 865-878, 880-888, 890-894, 897-909, 911-921, 923-927, 930-943, 945-956, 958-961, 964-976, 978-988, 990-993, 996-1009, 1011-1022, 1024-1027, 1030-1042, 1044-1054, 1056-1059, 1062-1075, 1077-1088, 1090-1094, 1097-1112, 1114-1121, 1123-1127, 1130-1146, 1148-1156, 1158-1162, 1165-1177, 1179-1191, 1193-1197, 1200-1213 and 1215-1227;

Claims now amended include: claims 826, 828, 843, 845, 855-856, 858, 874, 886-890, 905, 918, 920-921, 923, 939, 953, 955-956, 972, 985, 987-988, 1005, 1018, 1020, 1022, 1038, 1051, 1053-1054, 1084, 1086, 1088, 1090, 1108, 1120-1121, 1123, 1142, 1154-1156, 1158, 1173, 1186, 1188, 1191, 1193, 1209, 1223 and 1225;

Claims now canceled include: claims 827, 833-834, 848, 857, 863-864, 879, 889, 895-896, 910, 922, 928-929, 944, 957, 962-963, 977, 989, 994-995, 1010, 1023, 1028-1029, 1043, 1055, 1060-1061, 1076, 1089, 1095-1096, 1113, 1122, 1128-1129, 1147, 1157, 1163-1164, 1178, 1192, 1198-1199 and 1214; and

Claims added include: None.

Entry of the above listing and claim amendments is respectfully requested.

Enz-5(D6)(C2)

Before addressing the claim amendments and the issues that were discussed at the August 12, 2004 interview, Applicants wish to express their sincere gratitude for the courtesy and time extended by Examiner Ardin H. Marschel, Ph.D., Group Art Unit 1631, to Applicants' representative, Eugene C. Rzucidlo, Esq. of the law firm, Greenberg Traurig, LLP, and their undersigned attorney.

I. Summary of August 12, 2004 PTO Interview

A. Claim 956 (Enablement Rejection, 7/14/04 Office Action, pp. 4-5)

Applicants' undersigned attorney noted at the beginning of the discussion that claim 956 inadvertently recited the term "sugar moiety" instead of "furanosyl moiety." He indicated that claim 956 would be amended to recite "furanosyl moiety" in response to the enablement rejection in the July 14, 2004 Office Action. The Examiner acknowledged Applicants' offer to amend claim 956.

B. Claims 855 et al. (Vagueness and Indefiniteness, 7/14/04 Office Action, p 3)

The matter of claims 855, 886, 920, 955, 987, 1020, 1053, 1086, 1120, 1154, 1188 and 1125 was discussed next. Applicants' attorney indicated that after reviewing the previous office action mailed on November 26, 2003, he took the Examiner's statement on page 3 regarding "further comprising" language as a possible means for amending the rejected claims that would overcome the rejection. The Examiner replied that the rejection required more than the amendment of these claims to recite that the claimed polymer further comprised the recited deoxyribonucleotide or ribonucleotide. In the case of these claims and the rejection, the Examiner said he thought that the rejected dependent claims expanded rather than limited the subject matter of the independent claims. Although no specific language was discussed at the interview, the Examiner did

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suggest looking into the possibility of reciting the polymer in a different way that might avoid the interpretation that the subject matter of the dependent claims was being broadened over the independent claims. To this, Applicants' attorney replied that he understood better the Examiner's position on the issue and that amendments to overcome the rejection would be made in the next response.

C. Claims 826 et al. (Vagueness and Indefiniteness, 7/14/04 Office Action, p 3)

The issue of the nucleotide analogs and their various characteristics with respect to incorporation and hybridization was discussed next. Applicants' attorney referred to a related application, Serial No. 08/486,069, in which the same matter was recently discussed. He indicated that he thought agreement had been reached in Serial No. 08/486,069 regarding the language for "nucleotide analog." Applicants' attorney also mentioned some of the points or evidence that had been offered or submitted including numerous instances of support in the specification for "nucleotide analog" or "base analog." Applicants' attorney also pointed to Kornberg's DNA Replication textbook and Dr. Scheit's book titled Nucleotide Analogs." In response to these remarks, the Examiner suggested that the next response should point to the record in this case and in related Serial No. 08/486,069. Applicants' attorney noted that copies of relevant pages from Dr. Kornberg's book and a complete copy of Dr. Scheit's book were submitted in an IDS for Serial No. 08/486,069. Applicants' attorney also indicated that the Kornberg pages and Scheit copy were probably already of record in this application.¹ The Examiner suggested that the record in this application be clarified with respect to the "nucleotide analog" issue.

¹ Following the August 12, 2004 interview, Applicants' attorney confirmed that 38 documents, including the Kornberg pages and Scheit copy, were submitted in their April 29, 2004 Supplemental Information Disclosure Statement Under 37 C.F.R. §§1.56 and 1.97-1.98. These 38 documents correspond to and are identical to 38 documents submitted in Applicants' May 23, 2000 IDS filed in related Serial No. 08/486,069.

D. Claims 826-1227 (Written Description, 7/14/04 Office Action, p. 2)

The rejection of the claims for the lack of written description support for the term "non-nucleotidyl" was discussed next. Applicants' attorney indicated that he thought that support for this language was provided in their April 2004 Amendment, adding that the suggestion for "non-nucleotidyl" came from the Examiner. In reply, the Examiner noted that any claim amendments, whether suggested by the patent examiner, or made solely by the applicants, must find support in the disclosure. Applicants' attorney outlined some elements of support for "non-nucleotidyl," and the Examiner urged that such support be included in the next response. Before closing on the subject of "non-nucleotidyl," Applicants' attorney mentioned a couple of legal cases dealing with negative limitations. He noted that in one case, Ex parte Parks, two declarations had been submitted in support of the negative language, and that the Board of Patent Appeals & Interferences took note of the declarations in its opinion that found the negative language supported. The Examiner replied that he would consider a declaration on this matter if it was submitted. Applicants' attorney indicated that he would look into submitting such a declaration from an expert [having ordinary skill in the art].

E. Anticipation Rejection (Based on Dunn et al. (1977) or Hung US 4,224,408)

The previous prior art rejections based on Dunn's 1977 Cell paper and Hung's U.S. Patent No. 4,224,408 were discussed next. The Examiner reiterated his position that he thought that the definition of the non-radioactive Sig label moiety without the non-nucleotidyl limitation was broad enough to be anticipated by Dunn or by Hung. According to the Examiner, this would include Dunn's SV40 RNA tail and Hung's cDNA polymer. Applicants' representative mentioned that the Dunn paper stated in the "Experimental Procedures" section that adenovirus and SV40 were both labeled in vitro with $\alpha^{32}\text{P}$ -nucleotides. The Examiner

acknowledged this statement and he reiterated that the labeling method disclosed by Dunn could be addressed in the next response, if desired [by Applicants].

F. Anticipation Rejection (Based on Hartman et al. (1981))

The last issue discussed at the August 12, 2004 interview was the prior art anticipation rejection of several claims by Hartman's 1981 paper. Applicants' attorney noted that the Hartman paper disclosed an azo group attached to the pyrimidine base of a nucleotide or an RNA polymer. He also noted that the rejected present claims are all directed to a non-radioactive Sig label moiety attached to the phosphate moiety of a nucleotide in a DNA or RNA polymer. The Examiner acknowledged this statement, but he went on to say that in Hartman's paper the azo group on the base could be considered a label, as could the entire nucleotide in which the azo group is present. After some further discussion on this point, including the possibility of amending the claims to recite "at least three carbons," the Examiner seemed willing to consider that reciting both "non-nucleotidyl" and "three carbons" in the independent claims might be sufficient to overcome the anticipation rejection by Hartman.

In concluding the interview, the Examiner requested that Applicants provide a general discussion of the interview summary in their response to the July 14, 2004 Office Action. Thus, the above is Applicants' summary of the August 12, 2004 interview.

II. Changes to the Claims

As indicated above, a number of claims have been amended. These amendments include the following:

(A) Amendments To The Independent Claims

(i) *Insertion of "three carbons" into the independent claims*

Each of the independent claims (826, 856, 888, 921, 956, 988, 1022, 1054, 1088, 1121, 1156 and 1191) has been amended to recite that the non-radioactive Sig label moiety comprises "at least three carbon atoms." The previous dependent claims directed to Sig comprising "at least three carbon atoms" have been canceled. The canceled dependent claims include claims 827, 857, 889, 922, 957, 989, 1023, 1055, 1122 and 1192.

(ii) *Transposition of the Sig non-radioactive label moiety*

In the case of several independent claims that include the sugar structure (claims 856, 921, 988, 1054, 1121 and 1191), the recitation for the Sig non-radioactive label moiety has been moved "higher up" in the claim, so to speak. Thus, in claim 856, for example, after the description for x, y and z, the language recites wherein Sig *comprises a non-polypeptide, non-nucleotidyl, non-radioactive label moiety which comprises at least three carbon atoms . . .* It is believed that the foregoing amendments to claims 856, 921, 988, 1054, 1121 and 1191 improves the readability by reciting Sig more positively and less inferentially in the language of these six independent claims.

(iii) *Amendment of claim 956 to recite "furanosyl moiety"*

In response to the enablement rejection, claim 956 has been amended to recite "furanosyl moiety" instead of "sugar moiety." As explained at the August 12th interview, the previous "sugar moiety" recitation in claim 956 was inadvertent

and altogether unintended, particularly since all other independent claims recited "furanosyl moiety." See also Applicants' April 23, 2004 Amendment, page 86, first paragraph.

(iv) Deletion of "saccharide component" in Sig members

In four independent claims (956, 988, 1022 and 1054), the term "saccharide component" has been deleted. This change has also been effected to eight dependent (claims 828, 858, 890, 923, 1090, 1123, 1158 and 1193).

(v) Correction of minor or obvious errors

In eleven independent claims (826, 856, 921, 956, 988, 1022, 1054, 1088, 1121, 1156 and 1191), the phrase "or modified nucleotide analog" has been inserted in one instance. This correction conforms to the language in the preamble of the claim which recites "comprising at least one modified nucleotide *or modified nucleotide analog* having the formula . . ."

In claim 888, an inadvertent recitation of "non-nucleotidyl" has been deleted and inserted later between "non-polypeptide" and "non-radioactive."

In claim 1054, three inadvertent instances where the word "of" appears in the recitation of x, y and z have been corrected.

B. Amendments To The Dependent Claims

(i) Change from "furanosyl" moiety to "PM" or "phosphate" moiety

In eleven dependent claims (843, 874, 905, 939, 972, 1005, 1038, 1071, 1108, 1142, 1173 and 1209), the term "furanosyl moiety" has been changed to either "PM" or the "phosphate" moiety. Thus, claim 843 recites "wherein said Sig moiety is attached to the PM of a terminal nucleotide in said oligo- or polydeoxyribonucleotide;" and claim 874 recites "wherein said Sig moiety is

attached to the PM of a terminal nucleotide in said oligo- or polydeoxyribonucleotide."

(ii) Change to "comprises"

In claims 845, the word "comprises" has been substituted for "has." Thus, claim 845 now recites "wherein the furanosyl moiety of said terminal nucleotide *comprises* an oxygen atom at the 2' position thereof."

(iii) Amendments to clarify deoxy-type oligomers or polydeoxyribonucleotides

In response to the vagueness and indefiniteness rejection (July 14, 2004 Office Action, page 3, third full paragraph), several dependent claims have been amended to clarify the language of the nucleic acid polymer. The amended claims include the following twenty dependent claims: 855, 886, 918, 920, 953, 955, 985, 987, 1018, 1020, 1051, 1053, 1084, 1086, 1120, 1154, 1186, 1188, 1223 and 1225. In claim 855, for example, the language now recites "[a]n oligo- or polynucleotide comprising the oligo- or polydeoxyribonucleotide of claim 826, and further comprising at least one ribonucleotide." It is believed that the foregoing amendments clarify the relationship, for example, between the deoxy-type oligomers or polydeoxyribonucleotides and the dependent claims that recite a ribonucleotide. Moreover, it is believed that the amendments to these twenty dependent claims serve to further limit the subject matter claimed therein.

(iv) Correction of obvious misspellings

Claims 887 and 1155 have been amended to correct the misspelling of the word "polydexoyribonucleotide." Similarly, the misspelling of "deoxyribnucleotide" has been corrected above in each of claims 920, 987, 1053, 1086, 1188 and 1225.

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Entry of the above amendments is respectfully requested. No new issues are believed to be raised by the above claim amendments, nor are any of the amendments believed to require further consideration and/or search. Furthermore, the above claim amendments are not believed to raise any issue of new matter. Lastly, the amendments are believed necessary in order to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

III. July 14, 2004 Office Action

A. The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 826-1227 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In the July 14, 2004 Office Action (page 2), the Examiner stated:

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

NEW MATTER has been newly added to the claims due to the added "non-nucleotidyl" limitation directed to Sig moiety species. Applicants have not pointed to written basis as filed for this limitation nor has written basis as filed been found via consideration of the entirety of the instant disclosure as filed. It is acknowledged that numerous types of Sig moieties have been exemplified as filed, however, a clear delineation of such moieties to support the "non-nucleotidyl" limitation has not been found. All independent claims contain this NEW MATTER limitation. Claims which depend from independent claims either directly or indirectly also contain this NEW MATTER due to their dependence. This rejection is necessitated by amendment.

The rejection is respectfully traversed.

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Applicants respectfully submit that their specification fully supports the recitation of the non-radioactive Sig label moiety as *non-nucleotidyl*. Furthermore, their specification reasonably conveys that Applicants were in possession of such subject matter at the time their application was first filed in June 1982.

Applicants respectfully note that in each and every instance where it is described or even originally claimed in the specification, the Sig component is not a nucleotide or nucleotidyl in nature. A good description for Sig begins on page 96, last paragraph, and continues through the first paragraph on page 97. There, the '997 specification discloses:

The Sig moiety employed in the make-up of the special nucleotides of this invention could comprise an ***enzyme or enzymic material***, such as ***alkaline phosphatase, glucose oxidase, horseradish peroxidase*** or ***ribonuclease***. The Sig moiety could also contain a ***fluorescing component***, such as ***fluorescein*** or ***rhodamine*** or ***dansyl***. If desired, the Sig moiety could include a ***magnetic component*** associated or attached thereto, such as a ***magnetic oxide*** or ***magnetic iron oxide***, which would make the nucleotide or polynucleotide containing such a magnetic-containing Sig moiety detectable by magnetic means. The Sig moiety might also include an ***electron dense component***, such as ***ferritin***, so as to be available by observation. The Sig moiety could also include a ***radioactive isotope component***, such as ***radioactive cobalt***, making the resulting nucleotide observable by radiation detecting means. The Sig moiety could also include a ***haptén component*** or per se be capable of complexing with an antibody specific thereto. Most usefully, the Sig moiety is a ***polysaccharide or oligosaccharide or monosaccharide***, which is capable of complexing with or being attached to a sugar or polysaccharide binding protein, such as a lectin, e.g. Concanavilin A. The Sig component or moiety of the special nucleotides in accordance with this invention could also include a ***chemiluminescent component***.

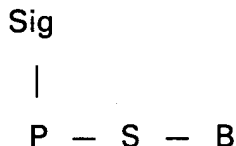
[emphasis added]

The above-quoted passage includes as many as 20 different examples for Sig. In none of these examples, however, is Sig described or even suggested to be a nucleotide or that it is nucleotidyl in nature.

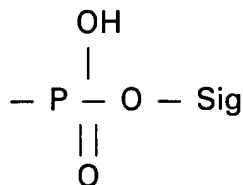
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In other portions of the originally filed specification, other descriptions for Sig are given. In each of these instances, it is clear that Sig is again a non-nucleotide or is non-nucleotidyl in nature. For example, in the last paragraph on page 94 and continuing through the top half of page 95, the specification discloses:

Still further, nucleotides in accordance with the practices of this invention include the nucleotides having the formula,



wherein P is the phosphoric acid moiety, S the sugar moiety and B the base moiety. In these special nucleotides the P moiety is attached to the 3' and/or the 5' position of the S moiety when the nucleotide is deoxyribonucleotide and at the 2', 3' and/or the 5' position when the nucleotide is a ribonucleotide. The base B is either a purine or a pyrimidine and the B moiety is attached from the N1 or the N9 position to the 1' position of the sugar moiety when said B moiety is a pyrimidine or a purine, respectively. The Sig chemical moiety is covalently attached to the phosphoric acid P moiety via the chemical linkage



said Sig, when attached to said P moiety being capable of signalling itself or making itself self-detecting or its presence known and desirably the nucleotide is capable of being incorporated into a double-stranded polynucleotide, such as DNA, RNA or DNA-RNA hybrid and when so incorporated therein is still self-detecting.

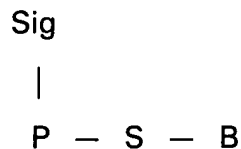
The fact that the passage above refers to "the nucleotide" being "capable of being incorporated into a double-stranded polynucleotide . . ." is significant because it establishes that Sig itself is not a nucleotide. If Sig were a nucleotide, then the passage would have to refer to -- at the very least -- a dinucleotide or some other polymeric nucleic acid structure, such as an oligonucleotide or a polynucleotide.

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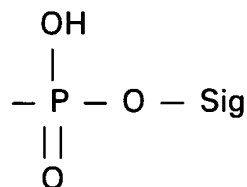
Instead, the passage specifically refers to "the nucleotide," thus clearly establishing that Sig itself is not a nucleotide.

Applicants further note that the originally filed claims support the description of Sig as a non-nucleotide or as non-nucleotidyl in nature. For example, original claim 141 recites:

A nucleotide having the general formula



wherein P is the phosphoric acid moiety, S the sugar moiety and B the base moiety, the phosphoric acid moiety being attached to the 3' and/or the 5' position of the sugar moiety when said nucleotide is deoxyribonucleotide and at the 2', 3' and/or 5' position when said nucleotide is a ribonucleotide, said base B being a purine or pyrimidine, said base B moiety being attached from the N1 or the N9 position to the 1' position of the sugar moiety when said base B is a pyrimidine or a purine, respectively, and wherein Sig is a chemical moiety is covalently attached to the phosphoric acid moiety via the chemical linkage



said Sig, when attached to said phosphoric acid moiety P being capable of signalling itself or making itself self-detecting or its presence known.

Because claim 141 is directed in its preamble to a nucleotide, it is clear that Sig cannot be a nucleotide or nucleotidyl by nature. To assert otherwise would be contrary to the original language in claim 141.

There are still further other instances in the specification where after the attachment of Sig to the phosphate moiety, the resulting composition is specifically

referred to as a *nucleotide*. Three such instances are found on pages 95 and 96 in the specification, and these are quoted below.

The Sig chemical moiety is covalently attached to the phosphoric acid P moiety (PM) via the [phosphate] chemical linkage . . . said Sig, when attached to said P moiety (PM) being capable of signalling itself or making itself self-detecting or its presence known and desirably ***the nucleotide*** is capable of being incorporated into a double-stranded polynucleotide . . .

[Page 95, lines 2-13; emphasis added]

The chemical moiety Sig so attached to the nucleotide P-S-B (PM-SM-BASE) is capable of rendering or making the ***resulting nucleotide***, now comprising P-S-B (PM-SM-BASE) with the Sig moiety being attached to one or more of the other moieties, self-detecting or signalling itself or capable of making its presence known per se, when incorporated into a polynucleotide. . .

[Page 96, lines 12-20; emphasis added]

The Sig moiety desirably should not interfere with the capability of ***the nucleotide*** to form a double-stranded polynucleotide containing the ***special Sig-containing nucleotide*** in accordance with this invention and, when so incorporated therein, the ***Sig-containing nucleotide*** is capable of detection, localization or observation.

[Page 96, lines 22-28; emphasis added]

Again, it is significant that after attachment of Sig to a nucleotide, the resulting composition is referred to in the passages above as "the nucleotide," "the resulting nucleotide," and "the special Sig-containing nucleotide." If Sig were a nucleotide or nucleotidyl, the above passage would not make any scientific sense because the resulting composition would itself not be a nucleotide. Clearly, however, the resulting composition is a nucleotide as seen by the reference in these three instances to "the nucleotide," "the resulting nucleotide," and "the special Sig-containing nucleotide."

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Finally, Applicants respectfully submit that their specification reasonably conveys to a person of ordinary skill in the art that they were in possession of the claimed subject matter wherein Sig comprises a *non-nucleotidyl* component. Submitted herewith and attached as Exhibit 1 is the Declaration of Dr. Alex A. Waldrop, III, who concludes as an expert and as a person of ordinary skill in the art, that the specification reasonably conveys to him that the claimed Sig comprises a non-nucleotidyl component. Applicants respectfully request that consideration be given to the evidence given in Dr. Waldrop's Declaration (Exhibit 2).

B. The Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 826-1227 are rejected under 35 U.S.C. 112, first paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the July 14, 2004 Office Action (page 3), the Examiner stated:

The independent claims as presently pending continue to cite analogs with various characteristics directed to DNA or RNA incorporation and also characterized as not substantially interfering with double helix formation or nucleic acid hybridization. The metes and bounds of the chemical structure of such characterized analogs has not been set forth and thus is still vague and indefinite as to what metes and bounds of such analog chemical structures correspond to the above noted characteristics. All independent claims contain these unclear limitations. Claims which depend from independent claims either directly or indirectly also contain this unclarity due to their dependence. This rejection is necessitated by amendment.

The vagueness and indefiniteness set forth in the previous office action, mailed 11/26/03, directed to the conflict between independent claims citing deoxy-type oligomers or polydeoxynucleotides vs. dependent claims requiring a ribonucleotide in the claimed composition is reiterated from the previous office action as still a conflict in the newly added claims. This is an issue in dependent claims 855, 886, 920, 955, 987, 1020, 1053, 1086, 1120, 1154, 1188, and 1125 vs.

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respective independent claims or internally within the claims wherein a polydeoxyribonucleotide, for example, further comprises a ribonucleotide or vice versa.

This rejection is necessitated by amendment.

The rejection is respectfully traversed.

Regarding the issue of "nucleotide analog" cited in the above rejection, Applicants respectfully point out that a full description of support and clarification of the meaning for this term was provided in several pages in their April 23, 2004 Amendment. See April 23, 2004 Amendment, page 78, last paragraph, continuing through page 85. In that discussion, Applicants provided:

- specification references to nucleotide analogs and/or base analogs (middle of page 79, continuing through the first two-thirds of page 81);
- reference to Dr. Arthur Kornberg's 1980 DNA Replication textbook (bottom third of page 81, continuing through the full paragraph on page 82);
- specification references to attachment, coupling and incorporation of nucleotide analogs and/or base analogs into DNA or RNA (page 82, last paragraph, continuing through the first half of page 85); and
- reference to Kornberg's 1980 DNA Replication textbook and to Dr. Karl Heinz Scheit's 1980 book titled Nucleotide Analogs: Synthesis and Biological Function (page 85, last paragraph; see also Footnote 3 on page 85).

As noted in Footnote 1 above, both the Kornberg pages and Scheit copy were submitted in Applicants' April 29, 2004 Supplemental Information Disclosure Statement.

Finally, on the analog issue, Applicants' attorney noted at the August 12th interview that the same matter had been addressed in connection with an amendment filed in May 2000 in their related application, Serial No. 08/486,069. Out of an abundance of caution and to make a full and complete record in this application for consideration by the Examiner, Applicants attorney is submitting herewith attached as Exhibit 2 a portion from Applicants' May 23, 2000 Amendment. The portion includes pages 187 through 217, and it references 38 exhibits that were submitted in IDS papers filed separately in related Serial No. 08/486,069 on May 23, 2000, and in the present application on April 29, 2004. Applicants respectfully request that consideration be given both to the information previously presented in their April 23, 2004 Amendment and the information provided above, as well as the previous information submitted in their May 23, 2000 Amendment for related Serial No. 08/486,069 (provided in part herewith as Exhibit 2).

With respect to the second half of the vagueness and indefiniteness rejection, Applicants believe that the rejection has been obviated by the above amendments to claims 855, 886, 918, 920, 953, 955, 985, 987, 1018, 1020, 1051, 1053, 1084, 1086, 1120, 1154, 1186, 1188, 1223 and 1225. See discussion above in Section II. B. (iii).

C. The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 956-987 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleotide containing embodiments wherein the sugar is a furanose moiety, such as ribose or deoxyribose, does not reasonably provide enablement for any generic sugar, such as cited in claim 956 etc. In the July 14, 2004 Office Action (pages 4-5), the Examiner stated:

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. . . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988).

The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

This rejection is maintained and reiterated from the previous office action, mailed 11/26/03, regarding claims still broadly citing sugar SM moieties directly or via dependence. This rejection has not been argued and is therefore maintained for reasons of record.

The enablement rejection is believed to have been rendered moot and irrelevant by the above amendments to claim 956 which now recites "furanosyl moiety" instead of "sugar moiety."

Reconsideration and withdrawal of the enablement rejection is respectfully request in view of the above amendments to claim 956.

D. The First and Second Anticipation Rejections Under 35 U.S.C. §102

In the Office Action (page 5), the Examiner stated: "The non-nucleotidyl limitation for the instant Sig moieties in the presently pending claims prevents a prior art rejections based on Dunn et al. [Cell 12:23 (1977)] or Hung (P/N

4,224,408), but removal of the NEW MATTER regarding such a limitation would require re-application of such a rejection.

As set forth above in response to the enablement rejection, Applicants believe that the term "non-nucleotidyl" used in defining the non-radioactive Sig label moiety is supported by their originally filed specification. Furthermore, the submitted Declaration of Dr. Alex A. Waldrop, III, an expert who is of ordinary skill in the art, establishes that Applicants' specification reasonably conveys that they were in possession of such "non-nucleotidyl" subject matter for the Sig component at the time their '997 application was originally filed in June 1982.

Accordingly, it is respectfully requested that the withdrawal of the anticipation rejections based on the Dunn and Hung documents be maintained.

E. The Third Anticipation Rejection Under 35 U.S.C. §102

Claims 888, 890, 903, 905, 907, 911, 919, 921, 923, 930, 931, 936, 937-939, 941, 943, 945, 951, 954, 956, 964, 965, 971, 972, 974, 978, 986, 988, 996, 997, 1002-1005, 1007, 1010, 1011, 1019, 1022, 1031, 1036-1038, 1043, 1044, 1052, 1054, 1062, 1063, 1068-1071, 1073, 1075, 1077, 1085, 1156, 1158, 1165, 1166, 1171-1173, 1175, 1177-1179, 1187, 1191, 1193, 1200, 1201, 1206-1208, 1121, 1214, 1215, 1221 and 1224 stand rejected under 35 U.S.C. §102(a) as being clearly anticipated by Hartmann et al. [Biopolymers 20:2635 (1981)].

As indicated in the previous prior art rejections, Applicants believe that the term "non-nucleotidyl" is supported by their specification and that the Declaration of Dr. Alex A. Waldrop, III submitted herewith, convincingly establishes that Applicants' specification reasonably conveys that they were in possession of such "non-nucleotidyl" subject matter at the time their application was originally filed (June 1982). Moreover, the inclusion of the "three carbon" limitation for the non-

radioactive Sig label moiety further distinguishes Applicants' claimed invention from Hartman's paper, a point that was also discussed at the August 12th interview.

Accordingly, in light of the above claim amendments, the above remarks directed to the new matter rejection and the declaration evidence being concurrently submitted with this paper (Exhibit 1), Applicants respectfully request that the anticipation rejection based on Hartman et al. be reconsidered and withdrawn.

Favorable action on this application is respectfully requested.

To The July 14, 2004 Office Action) -- September 3, 2004]

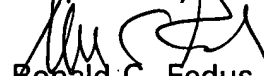
SUMMARY AND CONCLUSIONS

After entry of the complete listing of the claims above, the pending claims in this application include 826, 828-832, 835-847, 849-856, 858-862, 865-878, 880-888, 890-894, 897-909, 911-921, 923-927, 930-943, 945-956, 958-961, 964-976, 978-988, 990-993, 996-1009, 1011-1022, 1024-1027, 1030-1042, 1044-1054, 1056-1059, 1062-1075, 1077-1088, 1090-1094, 1097-1112, 1114-1121, 1123-1127, 1130-1146, 1148-1156, 1158-1162, 1165-1177, 1179-1191, 1193-1197, 1200-1213 and 1215-1227.

No fee or fees are believed due in connection with this paper which is being timely filed with a smaller number of claims being presented than were paid for previously. Concurrently filed with this Amendment is a Notice of Appeal and authorization for the large entity fee therefor. If any other fee or fees are due, however, either for this Amendment or the accompanying Notice of Appeal, The Patent and Trademark is authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, and to credit any overpayment thereto.

In view of the above discussion of the issues and submitted exhibits, Applicants respectfully submit that all of the pending claims are now in allowable condition. Should it be deemed helpful or necessary, the Examiner is respectfully invited to telephone the undersigned at (212) 583-0100 to discuss the subject application.

Respectfully submitted,



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